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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/751,056	01/02/2004	Gerianne Tringali DiPiano	FEM 104	1945
23579	7590	04/29/2010	EXAMINER	
Pabst Patent Group LLP			KIM, JENNIFER M	
1545 PEACHTREE STREET NE				
SUITE 320			ART UNIT	PAPER NUMBER
ATLANTA, GA 30309			1628	
			MAIL DATE	DELIVERY MODE
			04/29/2010	PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	10/751,056	DIPIANO ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	JENNIFER M. KIM	1628	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

1) Responsive to communication(s) filed on 10 February 2010.

2a) This action is **FINAL**.                            2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

4) Claim(s) 1,10,17 and 19 is/are pending in the application.

4a) Of the above claim(s) 10,17 and 19 is/are withdrawn from consideration.

5) Claim(s) \_\_\_\_\_ is/are allowed.

6) Claim(s) 1 is/are rejected.

7) Claim(s) \_\_\_\_\_ is/are objected to.

8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) All    b) Some \* c) None of:

1. Certified copies of the priority documents have been received.
2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

1) Notice of References Cited (PTO-892)

2) Notice of Draftsperson's Patent Drawing Review (PTO-948)

3) Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date 1/29/2010; 8/13/2009; 5/29/2009

4) Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_ .

5) Notice of Informal Patent Application

6) Other: \_\_\_\_\_.

## **DETAILED ACTION**

The amendment filed February 10, 2010 have been received and entered into the application.

Applicant's arguments with respect to claim 1 have been considered but are moot in view of the new ground(s) of rejection.

### **Claim Rejections - 35 USC § 103**

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of

the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 1 is rejected under 35 U.S.C. 103(a) as being unpatentable over Schreder et al. (US 2003/0153585 A1) in view of Ragavan et al. (U.S. Patent No. 5,993,856) of record.

Schreder et al. teach pharmaceutical preparations comprising at least one medicament active ingredient and **2-pyrrolidone** as solubilizer (abstract). Schreder et al. teaches that preference is given to medicament active ingredients which have low solubility in water ([0001]). Schreder et al. teach that the low-solubility medicament active ingredient includes **danazol** and it is suitable for the preparation [0016]). Schreder et al. teach that 2-pyrrolidone is employed as solubilizer ([0021]). Schreder et al. teach that the preparation can be formulated in the semisolid state such as **ointments or gel-like medicaments** ([0045]). Schreder et al. teach that 5 to 500mg of the medical active ingredients can be employed ([0058]). This range of amounts encompasses Applicant's effective amount of danazole disclosed in the specification on page 9 (under D. Dosage). Schreder et al. teach that the proportion of 2-pyrrolidone in the preparation is from 1 to 30 percent by weight [0059]). This range of amounts encompasses Applicants' amount of oleic acid interchangeable with 2-pyrrolidine as a

penetration enhancer illustrated as examples (see page 9 and examples) in the instant specification. Schreder et al teach that the solubility of a low solubility medicament active ingredients can be achieved by increasing dissolution rate, and that alcohols is a well known solubilizer which increases dissolution rate of the low-solubility medicament ([0005]-[0006]).

Schreder et al. do not expressly illustrate hydroalcoholic gel formulation comprising danazol.

Ragavan teaches that gel formulation of danazol is useful for topical or local delivery directly on reproductive organs such as female reproductive system (abstract, example). Ragavan teaches that it is desirable to administer the danazole formulations locally with dosages which are less than other modes of delivery, such as oral delivery. Transdermal doses are usually found to be one-quarter of the oral dose for similar efficacy. In this instance, it is possible to lower the dose even lower. Such dosage administration will ensure negligible or relatively low serum levels of danazol to avoid undesirable side effects associated with oral dosing, such as hirsutism and other androgenic side effects (column 7, lines 45-56). Ragavan teaches that cetostearyl alcohol can be employed as standard excipients (column 3, lines 15-37).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to formulate a drug formulation of danazol with 2-pyrrolidone in a gel formulation including hydroalcoholic gel because Schreder et al. teach that a medicaments with low solubility in water such as danazol can be formulated by employment of solubilizer such as 2-pyrrolidine in an ointment or gel-like medicament

and because 2-pyrrolidone as solubilizer dissolves the low-solubility medicament active agents such as danazol and semisolid pastes are formed. Moreover, Ragavan teaches that gel formulation of danazol is useful for topical or local delivery to female reproductive system and in transdermal use, the lower doses compared to oral doses can be used to avoid the undesirable side effects associated with oral dosing such as hirsutism and other androgenic side effects. One would have been motivated to make such a modification in order to successfully formulate topical danazole gel formulation without the undesirable side effects of the oral administration. With regard to the limitation of the hydroalcoholic gel is noted, however, the pharmaceutical forms, e.g., gel, hydrogel, hydroalcoholic gel etc; are all deemed obvious since they are all within the knowledge of the skilled pharmacologist and represent conventional formulations depends on the content of the formulations. One of ordinary skill in the art would readily recognized that danazol gel formulation of Schreder et al as modified by Ragavan can be formulated in hydroalcoholic gel because alcohol is a well known solubilizer of the low-solubility medicament such as danazol and that both Schreder and Ragavan teach alcohol can be employed in danazol formulations. For these reasons the claimed subject matter is deemed to fail to patentably distinguish over the state of the art as represented by the cited references. The claims are therefore properly rejected under 35 U.S.C. 103.

None of the claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

### **Communications**

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JENNIFER M. KIM whose telephone number is (571)272-0628. The examiner can normally be reached on Monday through Friday 6:30 am to 3 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/JENNIFER M KIM/  
Primary Examiner, Art Unit 1628

Jmk  
April 20, 2010